

---

---

# Correlation of American Burn Association Sepsis Criteria With the Presence of Bacteremia in Burned Patients Admitted to the Intensive Care Unit

---

Brian K. Hogan, MD,\*†‡ Steven E. Wolf, MD,\*†§  
Duane R. Hospenthal, MD, PhD,\*†‡ Laurie C. D'Avignon, MD,\*†‡  
Kevin K. Chung, MD,§ Heather C. Yun, MD,\*†‡ Elizabeth A. Mann, PhD, RN,§  
Clinton K. Murray, MD\*†‡

Severe burn injury is accompanied by a systemic inflammatory response, making traditional indicators of sepsis both insensitive and nonspecific. To address this, the American Burn Association (ABA) published diagnostic criteria in 2007 to standardize the definition of sepsis in these patients. These criteria include temperature ( $>39^{\circ}\text{C}$  or  $<36^{\circ}\text{C}$ ), progressive tachycardia ( $>110$  beats per minute), progressive tachypnea ( $>25$  breaths per minute not ventilated or minute ventilation  $>12$  L/minute ventilated), thrombocytopenia ( $<100,000/\mu\text{l}$ ; not applied until 3 days after initial resuscitation), hyperglycemia (untreated plasma glucose  $>200$  mg/dL,  $>7$  units of insulin/hr intravenous drip, or  $>25\%$  increase in insulin requirements over 24 hours), and feed intolerance  $>24$  hours (abdominal distension, residuals two times the feeding rate, or diarrhea  $>2500$  mL/day). Meeting  $\geq 3$  of these criteria should “trigger” concern for infection. In this initial assessment of the ABA sepsis criteria correlation with infection, the authors evaluated the ABA sepsis criteria’s correlation with bacteremia because bacteremia is not associated with inherent issues of diagnosis as occurs with pneumonia or soft tissue infections, and blood cultures are typically obtained due to concern for ongoing infections falling within the definition of “septic.” A retrospective electronic records review was performed to evaluate episodes of bacteremia in the United States Army Institute of Research from 2006 through 2007. A total of 196 patients were admitted during the study period who met inclusion criteria. The first positive and negative cultures, if present, from each patient were evaluated. This totaled 101 positive and 181 negative cultures. Temperature, heart rate, insulin resistance, and feed intolerance criteria were significant on univariate analysis. Only heart rate and temperature were found to significantly correlate with bacteremia on multivariate analysis. The receiver operating characteristic curve area for meeting  $\geq 3$  ABA sepsis criteria is 0.638 (95% confidence interval 0.573–0.704;  $P < .001$ ). Among severe burn patients, the ABA trigger for sepsis did not correlate strongly with bacteremia in this retrospective chart review. (J Burn Care Res 2012;33:371–378)

Infections remain a major cause of morbidity and mortality in burn patients.<sup>1</sup> Delays in diagnosis and treatment of infections have repeatedly been shown to lead to worse outcomes in various clinical

settings.<sup>2,3</sup> Sepsis refers to a clinical state of systemic inflammation that is often caused by infection. A traditional framework for identifying patients with sepsis has been the presence of a specific set of clinical criteria, which defines the systemic inflammatory response syndrome (SIRS), in combination with

From the \*San Antonio Military Medical Center (SAMMC), Texas; †Uniformed Services University of the Health Sciences, Bethesda, Maryland; ‡University of Texas Health Science Center at San Antonio; and §US Army Institute of Surgical Research (USAISR), San Antonio, Texas.

The opinions or assertions contained herein are the private views of the authors and are not to be construed as official or reflecting the views of the Department of the Army, Department of the Air Force, Department of Defense or the US Government. This work was prepared as part of their official duties and, as such, there is no copyright to be transferred.

Address correspondence to Clinton K. Murray, MD, Infectious Disease Service, San Antonio Military Medical Center, Brooke Army Medical Center, 3551 Roger Brooke Drive, Fort Sam Houston, Texas 78234.

Copyright © 2012 by the American Burn Association.  
1559-047X/2012

DOI: 10.1097/BCR.0b013e3182331e87

<b>Report Documentation Page</b>			Form Approved OMB No. 0704-0188		
<p>Public reporting burden for the collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden, to Washington Headquarters Services, Directorate for Information Operations and Reports, 1215 Jefferson Davis Highway, Suite 1204, Arlington VA 22202-4302. Respondents should be aware that notwithstanding any other provision of law, no person shall be subject to a penalty for failing to comply with a collection of information if it does not display a currently valid OMB control number.</p>					
1. REPORT DATE <b>01 MAY 2012</b>	2. REPORT TYPE <b>N/A</b>	3. DATES COVERED <b>-</b>			
<b>4. TITLE AND SUBTITLE</b> <b>Correlation of American Burn Association Sepsis Criteria With the Presence of Bacteremia in Burned Patients Admitted to the Intensive Care Unit.</b>			5a. CONTRACT NUMBER		
			5b. GRANT NUMBER		
			5c. PROGRAM ELEMENT NUMBER		
<b>6. AUTHOR(S)</b> <b>Hogan B. K., Wolf S. E., Hespenthal D. R., DâAvignon L. C., Chung K. K., Yun H. C., Mann E. A., Murray C. K.,</b>			5d. PROJECT NUMBER		
			5e. TASK NUMBER		
			5f. WORK UNIT NUMBER		
<b>7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)</b> <b>United States Army Institute of Surgical Research, JBSA Fort Sam Houston, TX</b>			8. PERFORMING ORGANIZATION REPORT NUMBER		
<b>9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)</b>			10. SPONSOR/MONITOR'S ACRONYM(S)		
			11. SPONSOR/MONITOR'S REPORT NUMBER(S)		
<b>12. DISTRIBUTION/AVAILABILITY STATEMENT</b> <b>Approved for public release, distribution unlimited</b>					
<b>13. SUPPLEMENTARY NOTES</b>					
<b>14. ABSTRACT</b>					
<b>15. SUBJECT TERMS</b>					
<b>16. SECURITY CLASSIFICATION OF:</b> a REPORT <b>unclassified</b>			<b>17. LIMITATION OF ABSTRACT</b> <b>UU</b>	<b>18. NUMBER OF PAGES</b> <b>8</b>	<b>19a. NAME OF RESPONSIBLE PERSON</b>
b ABSTRACT <b>unclassified</b>					
c THIS PAGE <b>unclassified</b>					

**Table 1.** SIRS criteria<sup>4,5</sup>

1. Temperature:  $>38^{\circ}\text{C}$  or  $<36^{\circ}\text{C}$
2. Heart rate:  $>90$  beats per min
3. Respiratory rate:  $>20$  breaths/min or  $\text{PaCO}_2 < 32 \text{ mm Hg}$
4. White blood cell count:  $>12,000$  or  $<4000 \text{ cells/mm}^3$

SIRS, systemic inflammatory response syndrome.

suspected infection (Table 1).<sup>4</sup> SIRS criteria are sensitive to the varying physiologic changes seen in different patient groups. Nearly, all patients with severe burns experience a sustained systemic inflammatory state during their acute illness, which make the use of traditional SIRS criteria difficult. More than half of trauma patients in some studies exhibit SIRS criteria without the presence of an ongoing infection.<sup>5,6</sup>

There is a need to establish the parameters that predict serious infection in burn populations. A number of clinical parameters and biomarkers have been and are being investigated but none have been found to be solely predictive of sepsis in burns.<sup>7-14</sup> The traditional SIRS criteria were previously examined in the 24 hours preceding blood culture in our institution. Absolute values or changes in temperature, white blood cell count, and neutrophil percentage were not found to be the clinically useful indicators of bloodstream infection.<sup>7</sup>

Recognizing the difficulties associated with applying the traditional SIRS criteria in burns, the American Burn Association (ABA) published revised burn-specific sepsis criteria in 2007 with a total of six variables to consider (Table 2).<sup>15</sup> The ABA indicates that meeting three criteria should “trigger” the clinician to consider the presence of a clinically significant infection and initiate empiric antibiotics. A patient would meet the definition of sepsis if these criteria were then coupled with a documented infection defined as a positive culture, a pathologic tissue source, or a clinical response to antimicrobials. As a pilot study, we attempted to evaluate the burn-specific ABA sepsis criteria in the 24 hours before obtaining blood cultures to determine whether they correlated with bacteremia in burn patients admitted to the intensive care unit (ICU). Although these criteria were formulated based on a limited number of studies in the adult and pediatric burn literature,<sup>16-18</sup> they have not been systematically evaluated to determine whether meeting the “trigger” correlates with sepsis. Bacteremia was selected as the sole dependent variable among other clinically significant infectious complications seen in burns (such as invasive wound infection and pneumonia) because of its relative fidelity as a diagnosis.

**Table 2.** ABA sepsis criteria<sup>15</sup>

Sepsis should be considered when three or more of the following criteria are met:

1. Temperature:  $>39^{\circ}\text{C}$  or  $<36.5^{\circ}\text{C}$
2. Progressive tachycardia:  $>110$  beats per min
3. Progressive tachypnea:
  - a.  $>25$  breaths per minute not ventilated
  - b. Minute ventilation  $>12 \text{ L/min}$  ventilated
4. Thrombocytopenia (not applied until 3 d after initial resuscitation):  $<100,000/\mu\text{l}$
5. Hyperglycemia (in the absence of preexisting diabetes mellitus)
  - a. Untreated plasma glucose  $>200 \text{ mg/dl}$  or equivalent mM/L
  - b.  $>7$  units of insulin/hr intravenous drip
  - c. Significant resistance to insulin ( $>25\%$  increase in insulin requirement over 24 hr)
6. Inability to continue enteral feedings  $>24$  hr
  - a. Abdominal distension
  - b. High gastric residuals (residuals two times feeding rate)
  - c. Uncontrollable diarrhea ( $>2500 \text{ ml/d}$ )

ABA, American Burn Association.

## METHODS

A retrospective electronic medical records review was performed to identify patients with burn injury admitted to the United States Army Institute of Research (USAISR) burn ICU from 2006 through 2007. The USAISR burn center serves the entire Department of Defense as well as south Texas.

Excision of full-thickness burns are performed by 7 to 10 days postburn. Topical antibiotics in use include mafenide acetate alternating with silver sulfadiazine, and perioperative antibiotics are typically intravenous vancomycin and amikacin. Patients are examined daily for signs of infection, and aggressive infection control measures are in place to minimize hospital-acquired infections. This study was conducted under a protocol approved by the Institutional Review Board of the Brooke Army Medical Center and the USAISR.

All adult patients who had blood cultures drawn during the study period were screened for the presence or absence of bacteremia or fungemia using the electronic healthcare laboratory system (Composite Health Care System database). The first positive and negative cultures from each patient were selected for analysis. Only patients admitted with thermal burns were included. Single blood cultures which recovered organisms known to be common skin contaminants (ie, diphtheroids, *Bacillus* spp., *Propionibacterium* spp., coagulase-negative *Staphylococcus* species, or micrococci) were excluded. The

indications for obtaining blood cultures varied by physician and clinical situation, although cultures were not obtained as a standard of care on admission or during predefined time periods during the hospitalization. Instead, blood cultures were drawn based on clinical concerns for bacteremia. More specifically, they included, but were not limited to, follow-up of previously bacteremic patients, hyperthermia and hypothermia, unexplained hypotension, organ dysfunction, and otherwise unspecified clinical deterioration. Cultures commonly were drawn through central venous and arterial catheters that were changed every 3 and 7 days, respectively, as a part of standard operating procedure. Patient data that were collected included age, gender, TBSA burned, presence of inhalation injury, and mortality. All clinical parameters pertaining to the ABA sepsis criteria (Table 2) and the SIRS criteria (Table 1) were collected from the electronic medical record (Essentris®, ClinComp, Intl., San Diego, CA) for the 24 hours preceding the time of blood culture collection. This included culture results, maximum and minimum temperature, heart rate, respiratory rate, minute volume if mechanically ventilated, use of high-frequency percussive ventilation (HFPV), platelet count, maximum and minimum white blood cell count, fasting blood glucose, maximum insulin drip rate, total insulin requirement, presence of enteral feeding intolerance, presence of abdominal distention, maximum gastric residuals, and stool volume. Evaluation included cultures during the initial 24 to 72 hours of admission as they are reflective of clinical parameters at the time of admission, although all six criteria are not applicable until after 72 hours of admission. Therefore, additional analysis was performed during time periods in which all triggers could be assessed.

Logistic regression was used to evaluate the relationship between the ABA sepsis criteria and the presence or absence of bacteremia. Further analyses were performed evaluating those patients with Gram-positive and Gram-negative bacteremia separately. Each clinical parameter comprising the ABA sepsis criteria and SIRS criteria was also evaluated individually with respect to bacteremia. The Pearson  $\chi^2$  test was used to compare categorical values. The Mann-Whitney *U* test was used to compare noncategorical values. A receiver operating characteristic curve (ROC) was constructed based on satisfying at least three ABA sepsis criteria with bacteremia as the outcome. A correlation coefficient between meeting the "trigger" and bacteremia was calculated. SPSS 16.0 for Windows (SPSS Inc., Chicago, IL) was used for all statistical analyses.

## RESULTS

During the period 2006 through 2007, 196 patients were admitted to the USAISR burn center who met inclusion criteria. The first positive and negative cultures from each patient were selected for analysis. Of note, not every patient had a corresponding positive or negative culture. This represented 101 positive and 181 negative cultures. Patient characteristics were compared between those with a positive blood culture and those with only a negative blood culture (Table 3). Most patients were young adult males, which reflect the demographics of active duty soldiers. The percent TBSA burned differed significantly between those with positive and only negative blood cultures (40.0 vs 22.0%;  $P < .001$ ). The median time from admission to the culture being drawn also differed between the groups (4 days vs 1 day;  $P < .001$ ). A greater number of patients with documented bacteremia also had inhalation injury (40.6 vs 25.2%;  $P = .023$ ) and were on mechanical ventilation (14.9 vs 4.2%;  $P = .012$ ). Mortality was also greater in those with documented

**Table 3.** Patient characteristics based on culture results

	Positive Blood Culture	Negative Blood Culture	<i>P</i>
N	101	95	
Age, yr (range)	27 (18–85)	31 (19–88)	.784
Male	91 (90.1)	84 (88.4)	.705
TBSA burn	40.0 (1.0–92.0)	22.0 (0.2–99.0)	.000
Full-thickness burns	26.0 (0–87)	9.5 (0–97.5)	.000
Diabetes mellitus	5 (4.9)	3 (3.2)	.527
Burned during combat operations in Iraq or Afghanistan	61 (60.4)	55 (57.9)	.722
Inhalational injury	41 (40.6)	24 (25.2)	.023
Respiratory rate/status			
HFPV	48 (47.5)	52 (54.7)	.314
CV	15 (14.9)	4 (4.2)	.012
NV	38 (37.6)	39 (41.1)	.624
Time to admission from burn (d)	2 (0–9)	2 (0–159)	.869
Time to culture from admission (d)	4 (0–41)	1 (0–14)	.000
<24 hr from admission	33 (32.7)	84 (88.4)	
24–72 hr from admission	11 (10.9)	6 (6.3)	
>72 hr from admission	57 (56.4)	5 (5.3%)	
Deaths	28 (27.7)	10 (10.5)	.002

Values are medians with range or percent.

HFPV, high-frequency percussive mechanical ventilation; CV, conventional mechanical ventilation; NV, no mechanical ventilation.

**Table 4.** Most commonly isolated bacterial pathogens

Bacteria	No. Pathogens From 101 Positive Blood Cultures
Gram-negative	74
<i>Acinetobacter calcoaceticus-baumannii</i> complex	29
<i>Klebsiella</i> spp.	15
<i>Pseudomonas aeruginosa</i>	13
<i>Enterobacter</i> spp.	7
<i>Serratia marcescens</i>	5
Other	9
Gram-positive	20
<i>Staphylococcus aureus</i>	14
<i>Streptococcus</i> spp.	6
<i>Enterococcus</i> spp.	4
Coagulase-negative <i>Staphylococcus</i>	3
Other	2
Mixed (Gram-positive and Gram-negative)	5
<i>Candida</i> spp.	2

More than one Gram-negative or Gram-positive organism were isolated from 14 cultures.

bacteremia (27.7 vs 10.5%;  $P = .002$ ). Of the 10 nonbacteremic patients who died, inhalational injury and/or respiratory failure was listed as a contributing cause of death in 7 of them. One patient had cirrhosis and disseminated intravascular coagulation. Another had abdominal compartment syndrome and small bowel necrosis complicating battle injuries. Only one had an infectious complication, which was a fungal wound infection leading to multiorgan failure.

Of the 101 positive blood cultures, the majority (74 cultures) grew Gram-negative bacteria (Table 4). Gram-positive organisms were isolated from 20 cultures. Five cultures were mixed with both Gram-positive and Gram-negative organisms, and

two cultures were positive for *Candida* spp. *Acinetobacter calcoaceticus-baumannii* complex, *Klebsiella* spp., and *Pseudomonas aeruginosa* were the most common Gram-negative organisms, while *Staphylococcus aureus* was the most common Gram-positive organism. The frequency of recovered organisms reflected what has been previously described in this population of patients.

The ABA sepsis criteria were analyzed categorically based on the presence of bacteremia (Table 5). Temperature, heart rate, insulin resistance, and feed intolerance criteria were significant on univariate analysis. Multiple regression was then performed including all six criteria. Only heart rate and temperature were found to significantly correlate with bacteremia. The same analysis was performed using SIRS criteria (Table 6). Temperature and heart rate criteria were significant on univariate analysis, whereas only temperature was significant after multivariate analysis. To assess the application of all six ABA criteria, a separate analysis was performed excluding those cultures drawn within 72 hours of admission (Table 7). Based on this analysis, none of the criteria were found to correlate with bacteremia.

The clinical parameters that make up each criterion were also analyzed either as continuous or categorical variables (Table 8). On this univariate analysis, maximum temperature but not minimum temperature was found to be significant as was heart rate. Bacteremic patients also had a greater insulin requirement, a larger stool volume, and were more likely to have abdominal distention. High feed residuals and white blood cell count did not differ between the two groups. On multivariate analysis, only maximum temperature, platelet count, maximum insulin drip rate, and abdominal distention were found to be significant.

ROC curve analysis was performed for the ABA sepsis (Figure 1) criteria to further assess the correlation

**Table 5.** Logistic regression of the individual American Burn Association sepsis criteria by the presence of bacteremia

Criteria	Positive Blood Culture (n = 101)	Negative Blood Culture (n = 188)	Univariate <i>P</i>	Multivariate		
				<i>P</i>	OR	95% CI
I (temperature)	74 (73.3)	92 (48.9)	.000	.003	2.301	1.328–3.987
II (heart rate)	96 (95.0)	150 (79.8)	.001	.006	4.051	1.487–11.036
III (respiratory rate)	88 (87.1)	147 (78.2)	.063	.234	0.645	0.314–1.327
IV (platelets)	9 (8.9)	16 (8.5)	.908	.440	1.448	0.566–3.702
V (insulin resistance)	35 (34.7)	35 (18.6)	.002	.062	0.564	0.309–1.030
VI (feed intolerance)	26 (25.7)	29 (15.4)	.033	.070	0.555	0.294–1.048

Values are number of cultures (%) that met each criterion.

OR, odds ratio; CI, confidence interval.

**Table 6.** Logistic regression of the individual systemic inflammatory response syndrome criteria by the presence of bacteremia

Criteria	Positive Blood Culture (n = 101)	Negative Blood Culture (n = 188)	Multivariate			
			Univariate <i>P</i>	Multivariate <i>P</i>	OR	95% CI
Temperature	82 (81.2)	104 (55.3)	.000	.000	3.128	1.747–5.602
Heart rate	101 (100)	179 (95.2)	.025	.999	0.000	0.000
Respiratory rate	43 (42.6)	75 (39.9)	.658	.864	0.956	0.573–1.595
White blood cell count	48 (47.5)	79 (42.0)	.369	.358	0.788	0.475–1.309

Values are number of cultures (%) that met each criterion.

OR, odds ratio; CI, confidence interval.

with bacteremia. The ROC curve area for meeting  $\geq 3$  criteria is 0.638 (95% confidence interval 0.573–0.704;  $P < .001$ ) (Figure 1). Seventy-nine of 101 positive cultures (78.2%) met the trigger, while 95 of 188 negative cultures (50.5%) met the trigger. The sensitivity and specificity were 78.2 and 49.5%, respectively. The positive predictive value was 45.4%. The negative predictive value was 80.9%. The correlation coefficient between meeting the trigger of  $\geq 3$  criteria and bacteremia was 0.270 ( $P < .001$ ).

## DISCUSSION

The purpose of the ABA consensus conference in 2007 was to create a standardized definition for sepsis specific for patients who had suffered severe burns. This was to provide uniformity for future study as well as provide some framework for clinical management. Although never systematically studied, traditional SIRS criteria were believed to be insufficient in the burn population. The selection of the various ABA sepsis criteria was based on a number of studies published in both the adult and pediatric burn literature. The hypermetabolic state caused by severe burn injury leads to alterations in the expected temperature,

heart rate, and respiratory rate. Higher values that might suggest sepsis were therefore selected. In pediatric burn patients, thrombocytopenia was found to be predictive of sepsis.<sup>17</sup> The hyperglycemia criterion was extrapolated from other patient populations. Feed intolerance was found to be an indicator of sepsis and mortality in a pediatric burn population.<sup>18</sup> In this study, we evaluated the correlation between the ABA sepsis criteria (and SIRS criteria) and bacteremia in a select subset of infected patients.

In this retrospective review of 282 blood cultures from 196 burn ICU patients, meeting  $\geq 3$  of 6 ABA sepsis criteria was not strongly correlated with bacteremia. When most criteria were generally evaluable (ie, after 72 hours), the findings were similar; however, results could have been affected by the small sample size. This was also true for SIRS criteria. As expected, the SIRS criteria were very common in this burn population.

Although the ABA criteria are established as dichotomous criteria to be used clinically in aggregate, we also evaluated each criterion individually to determine whether they correlated with bacteremia. Both the temperature and the heart rate criteria were fulfilled in a statistically greater number of bacteremic

**Table 7.** Logistic regression of the individual American Burn Association sepsis criteria by presence of bacteremia assessed >72 hr after admission

Criteria	Positive Blood Culture (n = 57)	Negative Blood Culture (n = 33)	Multivariate			
			Univariate <i>P</i>	Multivariate <i>P</i>	OR	95% CI
I (temperature)	47 (82.5)	22 (66.7)	.090	.300	1.784	0.597–5.336
II (heart rate)	54 (94.7)	25 (75.8)	.008	.051	4.349	0.996–18.984
III (respiratory rate)	48 (84.2)	31 (93.9)	.177	.179	0.296	0.050–1.748
IV (platelets)	5 (8.8)	5 (15.2)	.356	.481	0.602	0.147–2.466
V (insulin resistance)	29 (50.9)	17 (51.5)	.954	.987	1.008	0.379–2.680
VI (feed intolerance)	21 (36.8)	15 (45.5)	.424	.668	0.806	0.301–2.156

Values are number of cultures (%) that met each criterion.

OR, odds ratio; CI, confidence interval.

**Table 8.** Logistic regression of clinical parameters (including components of the ABA sepsis criteria and SIRS criteria) by the presence of bacteremia

Clinical Parameter	Positive Blood Culture	Negative Blood Culture	Univariate P	Multivariate		
				P	OR	95% CI
Temperature maximum (°C)	39.3 (35.8–41.0)	38.5 (32.5–40.7)	.000	.001	1.67	1.25–2.22
Temperature minimum (°C)	37.3 (29.5–39.4)	37.2 (27.8–40.1)	.121			
Heart rate	131 (104–172)	128 (69–178)	.002	.376		
Platelets (10 <sup>3</sup> /μl)	191 (22–756)	155 (23–915)	.040	.033	1.002	1.000–1.004
Insulin drip (units/hr)						
Maximum	4 (0–24)	1.8 (0–20)	.000	.009	1.08	1.02–1.15
Total	55 (0–346)	23.1 (0–380)	.000	.622		
Feed intolerance						
Distention	22 (21.8%)	18 (9.6%)	.004	.029	2.294	1.089–4.832
Stool volume	241 (0–4200)	77 (0–4200)	.000	.230		
High residuals (2 + feed rate)	7 (6.9%)	11 (5.9%)	.717			
White blood cell count	10.5 (0.7–27.1)	10.2 (2.1–46.0)	.979			

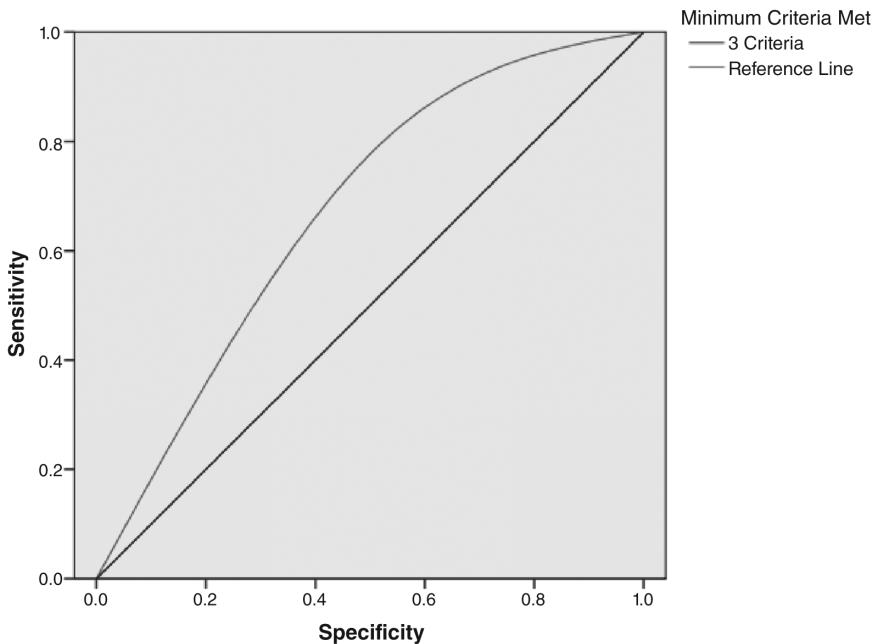
Values are medians (range) or numbers of cultures (%) that met each criterion.

ABA, American Burn Association; SIRS, systemic inflammatory response syndrome; OR, odds ratio; CI, confidence interval.

patients compared with nonbacteremic patients. When the SIRS criteria were evaluated, only the temperature criterion was found to be significantly associated with bacteremia. Temperature has classically served as an important marker of infection; however, its utility in this setting is unclear given the alterations in basal metabolic rate brought about by severe burn injury. Previously, in a study of similar patients admitted to the USAISR from 2001 to 2004, temperature was not found to be clinically useful in predicting bacteremia.<sup>7</sup> Our findings seem to be in contrast to these previous findings. However, when we evaluated temperature as a continuous variable, we found that although statistically higher in bacteremic patients (39.3°C vs 38.5°C,  $P < .001$ ), this small difference is unlikely to be clinically relevant. The clinical difference in heart rates between the two groups was also not significant. It should also be noted that several other variables that constitute the ABA sepsis criteria were found to be significant on univariate analysis when considered as continuous variables. Maximum insulin drip rate, abdominal distension, and stool volume were found to be significant. Perhaps, the ABA sepsis criteria need to be modified slightly. For example, maximum insulin drip rate before bacteremic episodes was an average of 4 units per hour compared with 1.8 units per hour when there was no bacteremia. A lower cutoff for the maximum insulin drip rate or for stool volume might be more appropriate.

The timing of the blood cultures that were included in this small retrospective study is important to consider. A significantly greater number of negative cultures were drawn within 1 day of admission

compared with positive cultures, which were drawn at a median time of 4 days. Temperature and heart rate criteria could still be measured. Assessment for tachypnea or increased minute ventilation could also be accomplished, although it is important to recognize that many patients were placed on HFPV early in their course (particularly when there was a concern for inhalational injury). It is unclear how ABA criteria should be applied in this setting. For the purposes of this study, when the mode of ventilation was HFPV, it was considered as fulfilling the progressive tachypnea criteria. The most significantly affected criterion based on timing of culture would be thrombocytopenia. This criterion would not apply until 3 days after initial resuscitation, thus potentially providing an additional evaluable criterion for the positive culture group. Hyperglycemia can be documented by three methods. First, a plasma glucose level was available for every patient and a fasting plasma glucose >200 mg/dl would fulfill this criterion. In addition, an intravenous insulin drip >7 units per hour or a 25% increase in the insulin requirement over 24 hours would also suffice. As many patients did not have insulin drips started immediately upon admission and there is typically no baseline insulin requirement, these last two methods of documenting hyperglycemia would not apply to most of the negative blood cultures drawn during the first 24 hours. Similarly, the ability to document feed intolerance may also be affected by the timing of the blood culture. Certainly, abdominal distention can be assessed in every patient. However, in those recently admitted in whom feeds had not been started yet,



**Figure 1.** Receiver operating characteristic curve for American Burn Association sepsis criteria.

inability to tolerate enteral feeds >24 hours could not be assessed. Also, feed residuals and stool volume were inconsistently documented in both groups but still more likely to be documented after the initial resuscitation when tube feeds and rectal tubes were placed. Again, these may provide additional ways to fulfill specific criteria in the positive culture group. When the ABA sepsis criteria were analyzed in only those with cultures obtained at least 72 hours after admission, none were found to be associated with bacteremia. This may be related to the small sample size. A larger prospective study would be required to adequately assess the impact of timing on the assessment of these criteria.

There are several limitations to this study. First, the study size was a significant limitation, which may have affected the ability to detect a difference between the groups. Second, the study was retrospective, and obtaining accurate data were dependent on complete and accurate documentation by the physicians and nurses who took care of the patients. There was also no clear guidance on ventilator modes such as HFPV and how their use should factor into the ABA sepsis criteria. Also, the role of antibiotics could not be accurately defined in this study as many patients were exposed to antibiotics both perioperatively and empirically for suspicion of infection. This would have the potential effect of decreasing blood culture sensitivity leading to some “true bacteremias” being included in the “negative culture”

group. Also, the common practice of drawing blood cultures through catheters may contribute to a small number of falsely positive cultures resulting from colonization of the catheter or contamination. Finally, the indication for drawing blood cultures was variable and not usually evident. Although blood cultures were generally drawn to evaluate possible bacteremia, other infectious processes that are not commonly associated with bacteremia (such as pneumonia and urinary tract infection) may have been underlying the patient’s change in status. This would in turn lead to a lower rate of positive blood cultures. We only assessed bacteremia and not all infections in this study which limits our ability to apply the ABA sepsis criteria to all infections in a burn population. Retrospectively, it was more difficult to distinguish colonization from true infection when evaluating cultures other than blood, and so these were not included. This does represent a significant limitation.

## CONCLUSIONS

In this small retrospective study, we found that meeting the  $\geq 3$  ABA sepsis criteria has a limited correlation with bacteremia in this burn ICU. As expected, the SIRS criteria were not found to be clinically useful as at least two criteria were satisfied in the majority of cases (84.8%). Of the clinical criteria defined by the ABA sepsis criteria, only temperature and

heart rate were found to be statistically significant. As individual clinical parameters, maximum temperature, platelet count, maximum insulin drip rate, and abdominal distention were found to be statistically significant. Further prospective studies of these and other clinical parameters with other infectious processes, especially in combination with other laboratory parameters such as procalcitonin, c-reactive protein, and/or erythrocyte sedimentation rate, are needed to gain a better understanding of markers of sepsis in this patient population.

## REFERENCES

- Church D, Elsayed S, Reid O, Winston B, Lindsay R. Burn wound infections. *Clin Microbiol Rev* 2006;19:403–34.
- Kollef MH, Sherman G, Ward S, Fraser VJ. Inadequate antimicrobial treatment of infections: a risk factor for hospital mortality among critically ill patients. *Chest* 1999;115:462–74.
- Ibrahim EH, Sherman G, Ward S, Fraser VJ, Kollef MH. The influence of inadequate antimicrobial treatment of bloodstream infections on patient outcomes in the ICU setting. *Chest* 2000;118:146–55.
- Levy MM, Fink MP, Marshall JC, et al.; SCCM/ESICM/ACCP/ATS/SIS. 2001 SCCM/ESICM/ACCP/ATS/SIS International Sepsis Definitions Conference. *Crit Care Med* 2003;31:1250–6.
- Muckart DJ, Bhagwanjee S. American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference definitions of the systemic inflammatory response syndrome and allied disorders in relation to critically injured patients. *Crit Care Med* 1997;25:1789–95.
- Salvo I, de Cian W, Musicco M, et al. The Italian SEPSIS study: preliminary results on the incidence and evolution of SIRS, sepsis, severe sepsis and septic shock. *Intensive Care Med* 1995;21 (Suppl 2):S244–S249.
- Murray CK, Hoffmaster RM, Schmit DR, et al. Evaluation of white blood cell count, neutrophil percentage, and elevated temperature as predictors of bloodstream infection in burn patients. *Arch Surg* 2007;142:639–42.
- Zhang B, Huang YH, Chen Y, Yang Y, Hao ZL, Xie SL. Plasma tumor necrosis factor-alpha, its soluble receptors and interleukin-1beta levels in critically burned patients. *Burns* 1998;24:599–603.
- Vindenes HA, Ulvestad E, Bjerknes R. Concentrations of cytokines in plasma of patients with large burns: their relation to time after injury, burn size, inflammatory variables, infection, and outcome. *Eur J Surg* 1998;164:647–56.
- Lobo SM, Lobo FR, Bota DP, et al. C-reactive protein levels correlate with mortality and organ failure in critically ill patients. *Chest* 2003;123:2043–9.
- Drost AC, Burleson DG, Cioffi WG Jr, Jordan BS, Mason AD Jr, Pruitt BA Jr. Plasma cytokines following thermal injury and their relationship with patient mortality, burn size, and time postburn. *J Trauma* 1993;35:335–9.
- Castelli GP, Pognani C, Cita M, Stuani A, Sgarbi L, Paladini R. Procalcitonin, C-reactive protein, white blood cells and SOFA score in ICU: diagnosis and monitoring of sepsis. *Minerva Anestesiologica* 2006;72:69–80.
- Brunkhorst FM, Eberhard OK, Brunkhorst R. Discrimination of infectious and noninfectious causes of early acute respiratory distress syndrome by procalcitonin. *Crit Care Med* 1999;27:2172–6.
- Barati M, Alinejad F, Bahar MA, et al. Comparison of WBC, ESR, CRP and PCT serum levels in septic and non-septic burn cases. *Burns* 2008;34:770–4.
- Greenhalgh DG, Saffle JR, Holmes JH, et al. American Burn Association consensus conference to define sepsis and infection in burns. *J Burn Care Res* 2007;28:776–90.
- Goldstein B, Giroir B, Randolph A. International pediatric sepsis consensus conference: definitions for sepsis and organ dysfunction in pediatrics. *Pediatr Crit Care Med* 2005;6:2–8.
- Housinger TA, Brinkerhoff C, Warden GD. The relationship between platelet count, sepsis, and survival in pediatric burn patients. *Arch Surg* 1993;128:65–6; discussion 66–7.
- Wolf SE, Jeschke MG, Rose JK, Desai MH, Herndon DN. Enteral feeding intolerance: an indicator of sepsis-associated mortality in burned children. *Arch Surg* 1997;132:1310–3, discussion 1313–4.